Frequency of serological non-responders and false-negative RT-PCR results in SARS-CoV-2 testing: a population-based study


Objectives The sensitivity of molecular and serological methods for COVID-19 testing in an epidemiological setting is not well described. The aim of the study was to determine the frequency of negative RT-PCR results at first clinical presentation as well as negative serological results after a follow-up of at least 3 weeks. Methods Among all patients seen for suspected COVID-19 in Liechtenstein (n=1921), we included initially RT-PCR positive index patients (n=85) as well as initially RT-PCR negative (n=66) for follow-up with SARS-CoV-2 antibody testing. Antibodies were detected with seven different commercially available immunoassays. Frequencies of negative RT-PCR and serology results in individuals with COVID-19 were determined and compared to those observed in a validation cohort of Swiss patients (n=211). Results Among COVID-19 patients in Liechtenstein, false-negative RT-PCR at initial presentation was seen in 18% (12/66), whereas negative serology in COVID-19 patients was 4% (3/85). The validation cohort showed similar frequencies: 2/66 (3%) for negative serology, and 16/155 (10%) for false negative RT-PCR. COVID-19 patients with negative follow-up serology tended to have a longer disease duration (p=0.05) and more clinical symptoms than other patients with COVID-19 (p<0.05). The antibody titer from quantitative immunoassays was positively associated with the number of disease symptoms and disease duration (p<0.001). Conclusions RT-PCR at initial presentation in patients with suspected COVID-19 can miss infected patients. Antibody titers of SARS-CoV-2 assays are linked to the number of disease symptoms and the duration of disease. One in 25 patients with RT-PCR-positive COVID-19 does not develop antibodies detectable with frequently employed and commercially available immunoassays.

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